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ORIGINAL ARTICLE

Effect of upper limb, lower limb and combined training on exercise performance, quality of life and survival in COPD

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KEYWORDS

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Abstract *Background:* Because there are differences between the upper limb (UL) and lower limb (LL) muscles in terms of the morphological and functional adaptations in COPD patients, specific protocols for strength training and endurance should be developed and tested for the corresponding muscle groups.

Aim: To elucidate the potential effects of unsupported UL and/or LL exercise training in patients with COPD. The 6-min walking distance (6-MWD), unsupported upper limb endurance (UULE) time, St. George's Respiratory questionnaire (SGRQ), BODE index and pulmonary function tests are used as outcome measures.

Methods: A prospective, randomized controlled study of patients with COPD. Patients were randomly assigned to one of 4 groups, group A received UL training, group B received LL training, group C received both UL and LL training and group D received no training (controls). Patients in group A, B, and C underwent exercise training 3 times weekly for 8 weeks. The outcome measures were carried out at study entry and after 8 weeks.

Results: 78 patients completed the study: 20 patients in group A, 21 in group B, 19 in group C and 18 in group D. Upper limb training significantly increased UULE time without affecting 6-MWD while LL training significantly increased 6-MWD without changing UULE time. Combined UL and LL training significantly increased both UULE time and 6-MWD. Significant reductions in the scores of SGRQ and BODE index were observed in groups A, B and C but not group D (control). No changes were found in pulmonary function in all groups at the end of the study.

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Conclusion: In patients with COPD, combined UL and LL training significantly enhanced the exercise tolerance and quality of life and reduced the risk of death (BODE index) without any change in the pulmonary function.

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Introduction

Systemic effects of COPD involve respiratory and skeletal muscles with loss of myosin heavy chain and elevated level of ubiquitin-conjugated proteins, suggesting accelerated muscle protein degradation [1]. The remaining contractile proteins in these fibres are dysfunctional, and the calcium sensitivity of force generation is reduced. These abnormalities could all contribute to muscle weakness [1].

Although patients with COPD have been reported to present with impaired lower limb (LL) and upper limb (UL) muscles, the morphological and functional adaptations appear to differ between these muscles. Celli et al. [2] were the first to compare LL and UL activities in patients with COPD showing that unsupported UL activities in COPD ended before LL exercises did. Patients with COPD frequently experience marked dyspnea and fatigue when performing simple UL activities [3]. Upper limb activities commonly require unsupported arm exercise, which poses a unique challenge for patients with COPD, whose UL muscles are required to act as accessory muscles of respiration. During unsupported arm exercise, the participation of the accessory muscles in ventilation decreases, and there is a shift of respiratory work to the diaphragm. This is associated with thoracoabdominal dyssynchrony, severe dyspnea, and termination of exercise at low workloads [4]. Regarding the lower limbs, reduced muscle strength and endurance are related to decreased muscle mass, decreased aerobic capacity, a predominance of glycolytic metabolism, and rapid accumulation of lactate during exercise, factors that might be responsible for early muscle fatigue in COPD patients [5].

The effectiveness of LL exercise training for patients with COPD has been well documented, with consistent clinically significant improvements in exercise capacity, symptoms, and quality of life [6]. Moreover, it has been seen that UL exercise training for patients with COPD increases UL work capacity, improves endurance, and reduces oxygen consumption at a given workload [7–9]. The benefits of combined UL and LL training, however, are less well defined. Therefore, the aim of this study was to measure exercise performance, quality of life and functional outcome by combining UL with LL exercises in patients with COPD.

Patients and methods

The patients were selected based on the criteria of the American Thoracic Society (ATS) for COPD: a history of smoking, X-ray findings, a medical history, and physical examination consistent with the diagnosis of COPD. Pulmonary function tests confirmed irreversible airflow obstruction, as measured by a forced expiratory volume in 1 s (FEV_1) < 80% of the predicted normal value [16] and a FEV_1 /forced vital capacity (FVC) ratio < 70%. All patients had a stable clinical condition at the time of study. Patients with coexistent diseases, such as

cardiovascular disease, diabetes, dementia, musculoskeletal problems, or vision difficulty, were excluded.

Protocol

A prospective, randomized controlled trial. Patients were randomly assigned to one of 4 groups, group A receiving UL training, group B receiving LL training, group C receiving both UL and LL training and group D receiving no exercise training (control group). Patients in group A and B underwent exercise training 3 times weekly for 8 weeks while patients in group C had UL and LL exercise training on alternate days.

1. *Upper limb exercise (30 min)*: This involved a 10-min warm-up period, 10-min of aerobic activity and 10-min cool-down. The aerobic activity included diagonal arm raises, arm abduction and elevation and reverse, and arm abduction, forward flexion, and reverse; and straight arm rises.
2. *Lower limb exercise (30 min)*: This involved a 10-min warm up, 10-min of cycling on an ergometric bicycle and 10-min cool down.
3. *Combined upper and lower limbs exercise*: This involved UL and LL exercise training on alternate days using the same protocols.

Outcome assessment

The followings were measured just before enrollment and at the end of the study:

1. *Unsupported upper limb endurance (UULE) time*: This was measured as previously described [10]. In brief; the patient was seated erect in a straight-backed chair with both feet on the floor facing the wall on which a chart was mounted. The chart consisted of eight horizontal colored strips of paper, the distance between the centers of the strips was 0.15 m. Each strip also had a clearly visible stage number. The first level was adjusted to be at the level of patient's knees by altering the position of the chart on the wall. The highest level the patient could reach was recorded. The patient held a light plastic bar (0.2 kg) and moved it during the exercise test. The test began with the patients lifting the bar from a neutral position to the first level, then the vertical amplitude of the lift increased by 0.15 m every minute as the patient progressed through the stages of the test. Once the patient reached maximum vertical height, the weight of the bar was progressively increased by 0.5 kg every minute to a maximum weight of 2 kg. Heart rate, dyspnea, and partial oxygen saturation were measured before and after the test. The test was terminated if the patient experienced dyspnea or arm fatigue at the maximum position reached. The endurance time was recorded.
2. *6-minutes walking distance (6-MWD)*: This was conducted in a hospital corridor as previously described [11]. During the test the patient was instructed to walk as fast as possible

for 6 min and to decrease speed or interrupt the test if experiencing severe dyspnea or any other limiting discomfort. Heart rate, dyspnea, and partial oxygen saturation were measured before and after the test. A minimal clinically significant difference in 6-MWD in patients with COPD was estimated to be 35 m [12].

3. *Health-related quality of life*: This was assessed by the St George's Respiratory Questionnaire (SGRQ) [13]. Each component of the questionnaire gives a weighted score between 0 and 100, including the total, with normal values in healthy individuals of < 7 for each component. A change of 4 points in the total score has been shown to represent a minimal clinically significant change [14].
4. *BODE index*: It is an index including 4 factors to predict the risk of death in COPD: the body mass index; BMI (B), the degree of airflow obstruction (O), the dyspnea (D), and exercise capacity (E) as assessed by the 6-MWD [15].
5. *Pulmonary function tests*: FVC, FEV₁, FEV₁/FVC, RV and TLC were measured using a computed unit (Jager, Germany) according to ATS guidelines [16].

Statistical methods

Categorical data were presented as numbers (percentage) while continuous variables were presented as mean (\pm standard deviation). One way ANOVA and χ^2 were used to compare continuous and categorical variables among groups respectively. Paired *t*-test was used within each group to assess whether a significant change from baseline had occurred. A *p* value < 0.05 was considered significant. Data were analyzed with the Statistical Package for Social Sciences (SPSS, Chicago, IL).

Results

Patients characteristics (Table 1)

Patients's age, gender, and BMI did not show any significant difference among the groups.

Outcome measures (Table 2)

There were no significant differences among the groups at baseline for any of the outcome variables.

1. *The unsupported upper limb endurance time*: The UULE time increased significantly after UL and combined training but not LL training nor in controls.
2. *6-minutes walk distance*: The 6-MWD increased significantly after LL and combined training but not UL training nor in controls.
3. *SGRQ total score*: A significant reduction in the total score of SGRQ was observed in the training groups i.e. A, B and C but not the control group (D).
4. *BODE index*: A significant decrease in the score of BODE index was observed in the training groups but not the control group.
5. *Pulmonary function tests*: No significant changes were observed in the parameters of the pulmonary function measured in all groups.

Discussion

This study shows that a physical exercise program designed to strengthen LL and UL muscles improves the exercise toler-

Table 1 Patients characteristics.

Group	A (n = 20)	B (n = 21)	C (n = 19)	D (n = 18)	P value
Age (years)	62 \pm 12	59 \pm 8	67 \pm 6	60 \pm 11	0.68 ^a
Males	18 (90%)	19 (90%)	17 (89%)	16 (89%)	0.87 ^b
BMI (kg/m ²)	24.2 \pm 3.8	25.4 \pm 4.2	23.7 \pm 6.1	24.9 \pm 4.9	0.16 ^a

BMI: body mass index.

^a One way ANOVA.

^b Chi square.

Table 2 Changes in outcome measures at the end of the study.

Group	A (n = 20)			B (n = 21)			C (n = 19)			D (n = 18)		
	Pre	Post	P	Pre	Post	P	Pre	Post	P	Pre	Post	P
UULE (seconds)	221 \pm 41	265 \pm 33	0.03	231 \pm 54	228 \pm 61	0.4	213 \pm 39	257 \pm 51	0.03	222 \pm 46	230 \pm 38	0.3
6-MWD (meters)	259 \pm 12	266 \pm 17	0.6	268 \pm 16	323 \pm 17	0.02	266 \pm 21	324 \pm 23	0.05	273 \pm 19	281 \pm 22	0.4
SGRQ	42 \pm 2.8	31 \pm 3.1	0.01	38 \pm 4.3	29 \pm 2.5	0.02	37 \pm 4.7	26 \pm 3.1	0.01	43 \pm 3.7	45 \pm 3.9	0.7
BODE	6 \pm 0.43	4 \pm 0.39	0.04	7 \pm 0.37	5 \pm 0.54	0.04	6 \pm 0.44	4 \pm 0.41	0.05	7 \pm 0.65	6 \pm 0.71	0.6
FEV ₁ %	43 \pm 2.3	45 \pm 3.4	0.6	46 \pm 4.1	48 \pm 3.9	0.4	41 \pm 3.7	43 \pm 2.1	0.4	45 \pm 3.5	45 \pm 4.8	0.6
FVC%	77 \pm 14.2	79 \pm 15.8	0.2	81 \pm 17.2	79 \pm 11.1	0.5	83 \pm 6.3	81 \pm 4.5	0.4	80 \pm 9.8	79 \pm 6.1	0.7
RV%	161 \pm 2.9	163 \pm 4.2	0.6	157 \pm 3.5	160 \pm 5.3	0.6	158 \pm 4.9	158 \pm 5.1	0.8	167 \pm 2.5	162 \pm 3.6	0.6

UULE: unsupported upper limb endurance time, 6-MWD: 6-min walk distance, SGRQ: total score of St. George respiratory questionnaire, BODE: BODE index, FEV₁: forced expiratory volume in one second, FVC: forced vital capacity, RV: residual volume.

ance, quality of life, and survival in patients with COPD without affecting the pulmonary function parameters.

The 6-MWD improved significantly following exercise training of LL. Minimal clinically significant difference in 6-MWD is defined as the smallest meaningful change, judged by the patient or experts, determined by questioning or observing the patient [17]. A recent analysis [12] of the interpretation of change in 6-MWD in patients with moderate-to-severe COPD (mean FEV₁, 39.2 ± 14.1%) comes from pooled data from 9 prospective trials. Using 3 statistical methods, they estimated a significant change in 6-MWD as 35 m, corresponding to a change of 10% from baseline 6-MWD. In this study, the mean change of 6-MWD was 55 and 58 m in group B and C, respectively. Limitation of exercise capacity is a hallmark of disability in COPD and is associated with poor health-related quality of life, increased morbidity, and higher mortality. [18–21]. Our data suggest that LL strengthening effectively improved exercise capacity as measured by 6-MWD. These findings are in agreement with several previously published studies of patients with COPD who received pulmonary rehabilitation [18,22–25]. The 6-MWD remained unchanged after UL training. Lake et al. [9], compared UL training with LL training and found that UL training improved arm function, but LL capacity was even decreased in that group; LL training and combined training increased 6-MWD. These findings could be explained by the fact that training effect is specific for the muscle group trained, with no cross-over benefit seen between the arms and legs [9]. Knox et al. [11], demonstrated a significant improved result on the repeated performance of a 6-MWD over a 4-week period that was mainly due to aerobic training effects and specificity of training.

The present study showed an improvement in UULE time after UL training, which is in accordance with study done by Epstein et al., who found that arm training resulted in increased UL endurance [26]. This might be due to improved synchronization and coordination of accessory muscle action during unsupported arm activity [27].

A significant reduction in the total score of SGRQ was observed in the groups A, B and C but not group D. The SGRQ has the advantage of being a standardized questionnaire, allowing comparison between studies and different interventions. A change of 4 points in the total score has been shown to represent the minimal clinically significant change [14]. Thus in our study, a reduction of the total score of >4 points at the end of 8 weeks clearly represents clinically significant benefits from our training. These findings are consistent with those observed by Griffiths et al. [28] where a mean improvement in total SGRQ score of 9.4 points was observed at 6 weeks, that remained significant at 4.8 points one year after an outpatient rehabilitation program. The reduction of the total score of SGRQ was mainly due to improvement of the dyspnea domain. This improvement in the dyspnea domain might be due to the psychological benefits of exercise, which included increased motivation, desensitization to dyspnea [29] and loss of fear of exercise.

A significant decrease was noted in the score of BODE index in groups A, B and C but not D (control). This index is useful being able to quantify the degree of pulmonary impairment (FEV₁), patients' perception of dyspnea (that predicts the likelihood of survival) [30], and the systemic consequences of COPD (6-MWD and BMI). These data are in agreement with the findings of Barakat et al. where a decrease of 2 points

(from 6 to 4) was noted in the score of the BODE index after UL and LL training [31].

The lack of changes in lung function parameters after training is not surprising. Reviewing the literature revealed that aerobic physical training did not modify lung function [6,29]. The FVC of an individual is dependent on lung elastic recoil, chest wall elasticity and respiratory muscle fitness. Exercises in our study are not designed to improve respiratory muscle stretching and have no effect on lung tissue structure.

Conclusion

Our study showed that UL and LL exercise training in COPD patients achieved a clinically significant increase in health-related quality of life and exercise tolerance and a decrease in the risk of death as measured using BODE index without any changes in the pulmonary function.

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